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Colorimetric Assay for *Exon 7 SMN1/SMN2* Single Nucleotide Polymorphism Using Gold Nanoprobes

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ABSTRACT

Introduction: Proximal spinal muscular atrophy (SMA) is one of the most significant neurodegenerative diseases amongst the autosomal-recessive genetic disorders which is caused by the absence of protein survival of motor neuron (SMN). A critical nucleotide difference in *SMN*2 compared to *SMN*1 gene leads to an inefficient protein. Hence, homozygous lack of *SMN*1 provides a progressive disease. Due to the high prevalence, up to now, several molecular diagnostic methods have been used which most of them are lengthy, expensive, and laborious. *Methods:* In the present study, we exploited a gold nanoprobe-based method for semi-quantitative *SMN*1 gene dosage analysis compared to *SMN*2. The assay was done under hybridization process between Au nanoprobes and different ratios of *SMN*1/*SMN*2 amplicons. *Results:* UV-vis spectra indicated that after the salt addition, nanoprobes aggregated gradually and their peak shifted to longer wavelengths except in the stable target-nanoprobes hybridization. The results revealed that the homozygous genotype of *SMN2* gene is distinguished from the heterozygous genotypes of *SMN* genes by the naked eye, whereas different ratio of heterozygous genotypes (*SMN1*/*SMN2)* are differentiated better from each other using peak analysis ratios. *Conclusion:* The presented strategy is an alternative simple method for discrimination of homozygous deletion of *SMN*1 in less than 30 min. However, further evaluation of the assay using clinical samples is recommended prior to real-world use.

Introduction

Proximal spinal muscular atrophy (SMA) is one of the most significant lethal neurodegenerative diseases amongst the autosomal-recessive genetic disorders.[1] This fetal-adolescent progressive illness is caused by the absence of protein survival of motor neuron (SMN). Homologous inverted copies of *SMN* genes (*SMN1* and *SMN2*), which are located on the chromosome 5q13, are responsible for protein expression. These copies differ by 5 nucleotide base pairs (one in *exon 7*, *exon 8*, and *intron 6*; two in *intron 7*). A critical single nucleotide polymorphism (SNP) in *exon 7* (840 C>T) leads to the production of defective form of SMN2 protein which consequently cannot circumvent the role of SMN complex, an assemblyosome of ribonucleoproteins.[2] As a result, homozygous deletion of *SMN1*, in 94% of SMA cases, leads to a progressive neuromuscular disease.[3]

Due to the high prevalence and carrier frequency (1 in 10,000 and 1 in 50, respectively), up to the present time, several molecular diagnostic methods have been developed for SMA detection. These techniques include: Linkage analysis,[4] Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP),[5,6] Amplification Refractory Mutation System-Polymerase Chain Reaction (ARMS-PCR),[7] PCR-single-strand conformation polymorphism (SSCP) analysis,[8]

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